REMARKS

Claims 22, 25-27, 29-48 are pending in the application.

Rejections Withdrawn

The Applicant notes that the previous rejections based on Mo et al.,(US 2004/0131664) and Okada et al. (US 2003/0220292) have been withdrawn because each of the cited references and the instant application were owned by or subject to an obligation of assignment to the same owner at the time the invention was made.

New Rejections

Claim Rejections under 35 U.S.C. §103(a)

Claims 22, 25-27, 29-48 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Yeager et al. (WO 01/51053, publication date 19 July 2001) in view of Kifor et al. (U.S. 5,958,884, issued on September 28, 1999 from application 09/047,594 filed March 25, 1998). The Applicant respectfully submits that the rejection under 35 U.S.C. §103(a) of Claims 22, 25-27, 29-48 is unwarranted and request that the rejection be withdrawn.

35 U.S.C. §103(a), quoted in the rejection, requires an evaluation of whether "the differences between the subject matter sought to be patented and the prior art are such that the ***subject matter as a whole*** would be obvious ***at the time the invention was made*** to a ***person having ordinary skill in the art*** to which said subject matter pertains. . ." (*emphasis added).* The subject matter as a whole reduces, then, to the distinguishing features clearly incorporated into the claims. *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459, 473 (1966). The Supreme Court has recently re-affirmed the *Graham* analysis. "[T]he scope and content of the prior art are ... determined; differences between the prior art and the claims at issue are ... ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1388 (U.S. 2007).

The Examiner Has Made No Finding of Fact Regarding The Level of Ordinary Skill In The Art

An inquiry into the level of ordinary skill in the art is one of the factual inquiries of the *Graham* analysis. No factual finding regarding the level of ordinary skill in the art has been made by the Examiner. The Applicant respectfully submits that the level of ordinary skill in the art would be that of a

clinician (M.D. or D.O.) treating patients suffering from sexual dysfunctions, including premature ejaculation, or that of a pharmaceutical chemist (Ph.D. or D.Sc.) seeking to develop a medication for the treatment of premature ejaculation.

The Examiner Has Made No Finding of Fact Regarding
The Scope and Content of the Prior Art at the Time the Invention Was Made

No factual finding regarding the scope and content of the prior art has been made by the Examiner beyond characterization of the teachings of the cited Yeager et al. reference and the Kifor et al. reference. The Office Action dated March 26, 2008 ("the Office Action") states that the Yeager et al. WO 01/51053 reference teaches a method of treating erectile dysfunction ("ED") and does not explicitly teach a method of treatment of premature ejaculation ("PE") comprising administering the pharmaceutical composition. Office Action page 4, lines 5-7. The Office Action further states that Kifor et al. teach erectile dysfunction is a disorder involving the failure of a male mammal to achieve erection, ejaculation, or both, and further teach that symptoms of erectile dysfunction include an ability to achieve or maintain an erection, ejaculatory failure, premature ejaculation, inability to achieve an orgasm (col. 4, lines 65-67, col. 5, lines 1-2). Office Action, page 4, lines 8-12.

> Erectile dysfunction is a disorder involving the failure of a male mammal to achieve erection, ejaculation, or both. Symptoms of erectile dysfunction include an inability to achieve or maintain an erection, ejaculatory failure, premature ejaculation, inability to achieve an orgasm. (Kifor et al., col. 4, lines 65-67, col. 5, lines 1-2).

The word "ejaculation" appears nowhere else in the Kifor et al. reference.

The Examiner thus points to the only two sentences in the Kifor et al. reference that address PE. Careful examination of these sentences leads to incongruous results, such as:

1. erectile dysfunction is a disorder that may or may not involve the failure to achieve erection;
2. erectile dysfunction is a disorder that may involve the failure to achieve ejaculation but does not involve the failure to achieve erection; and
3. symptoms of erectile dysfunction include ejaculatory failure, premature ejaculation, and inability to achieve an orgasm.

In contrast, the Yeager et al. reference states that erectile dysfunction is an inability of the male to achieve an erect penis as part of the overall multifaceted process of male sexual function (page 1, lines 16-20, citing the 1993 National Institutes of Health Consensus Development Statement on Impotence). The Yeager et al. reference provides detailed information on the condition of erectile dysfunction and various treatments, but does not state that erectile dysfunction involves the failure to achieve ejaculation.

The Office Action at page 4 admits "The reference teaches a method of treating erectile dysfunction and does not explicitly teach a method of treatment of premature ejaculation comprising administering the pharmaceutical composition." Indeed, the Yeager et al. reference does not mention premature ejaculation or any other sexual dysfunction other than erectile dysfunction.

The Examiner cites no other prior art on premature ejaculation or the treatment of premature ejaculation. Given the disparity between the Yeager et al. reference and the Kifor et al. reference in the definitions of erectile dysfunction, one of ordinary skill in the art of treating patients suffering from premature ejaculation would not combine the teachings of Yeager et al. and Kifor et al. to arrive at the presently claimed invention.

The Examiner further asserts that "one having ordinary skill in the art would have been motivated to administer the composition of Yeager in a method of treatment of premature ejaculation because of expectation of success and in achieving therapeutic benefits in treatment of sexual dysfunction." Office Action, sentence spanning page 4, lines 8-12. As noted above, no requisite finding as to level of ordinary skill in the art as been made, making the foundation of an assertion about the motivation and expectation of success of one of ordinary skill in the art questionable.

The Scope and Content of the Prior Art at the Time the Invention Was Made

The Applicant respectfully traverses the Examiner's characterization of the teachings of the cited Kifor et al. reference, and the assertion that one having ordinary skill in the art would have been motivated to administer the composition of Yeager et al. in a method of treatment of premature ejaculation because of expectation of success and in achieving therapeutic benefits in treatment of sexual dysfunction.

As noted in the application as filed, the diagnostic criteria for premature ejaculation (PE) as provided by the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV, 1994) are:

A. Persistent or recurrent ejaculation with minimal sexual stimulation before, on, or shortly after penetration and before the person wishes it. The clinician must take into account factors that affect duration of the excitement phase, such as age, novelty of the sexual partner or situation, and recent frequency of sexual activity.
B. The disturbance causes marked distress or interpersonal difficulty.
C. The PE is not due exclusively to the direct physiological effects of a substance (e.g. a drug or medication) or a general medical condition. American Psychiatric Association, Diagnostic and statistical manual of mental disorders, fourth edition. Washington, DC: American Psychiatric Association (1994).

Lu et al. US 2004/0241245, paragraph [0002]. As noted above, the definition of erectile dysfunction provided by the Yeager et al. reference states that erectile dysfunction follows that of the 1993 National Institutes of Health Consensus Development Statement on Impotence.

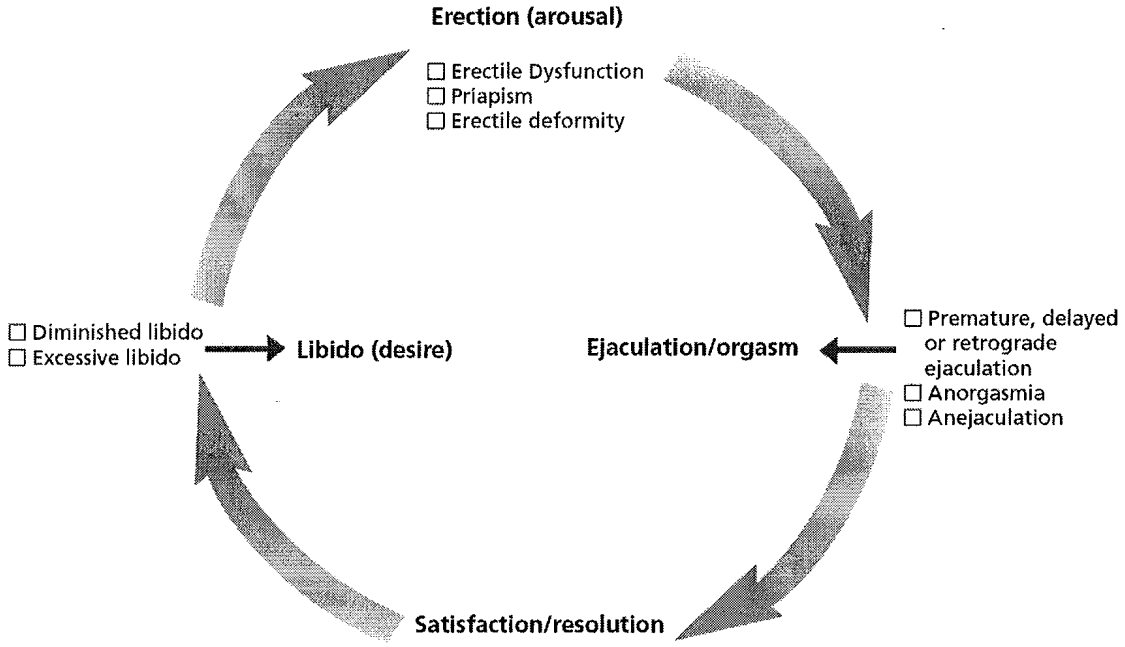

Figure 1, from Fine (2004), Figure 3

The four phases of the male sexual response cycle have been recognized by the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (Washington D.C., American Psychiatric Association, 1994, "DSM-IV"). As summarized by Fine (2004), the male cycle of sexual response (see Figure 1 above) can be divided into four phases: libido (desire), consisting of fantasies and thoughts about sexual activity and the desire to have sexual activity; erection (arousal), involving a subjective sense of sexual pleasure accompanied by physiologic changes, ie, penile tumescence and erection; ejaculation/orgasm, comprising a peaking in sexual pleasure, a sensation of ejaculatory inevitability, and ejaculation of semen; and satisfaction/resolution, consisting of a sense of muscular relaxation and general well-being. Fine SR, Erectile dysfunction and comorbid diseases, androgen deficiency, and diminished libido in men, *J. Am. Osteopath. Assoc.* 2004 Jan; 104(1 Suppl 1):S9-15. Sexual dysfunction is characterized by a disturbance in the processes that make up the cycle of sexual response, including: (libido/desire phase) diminished or excessive libido; (erection/arousal phase) erectile dysfunction, priapism, or erectile deformity; (ejaculation/orgasm phase) premature, delayed, or retrograde ejaculation; anorgasmia; or anejaculation.

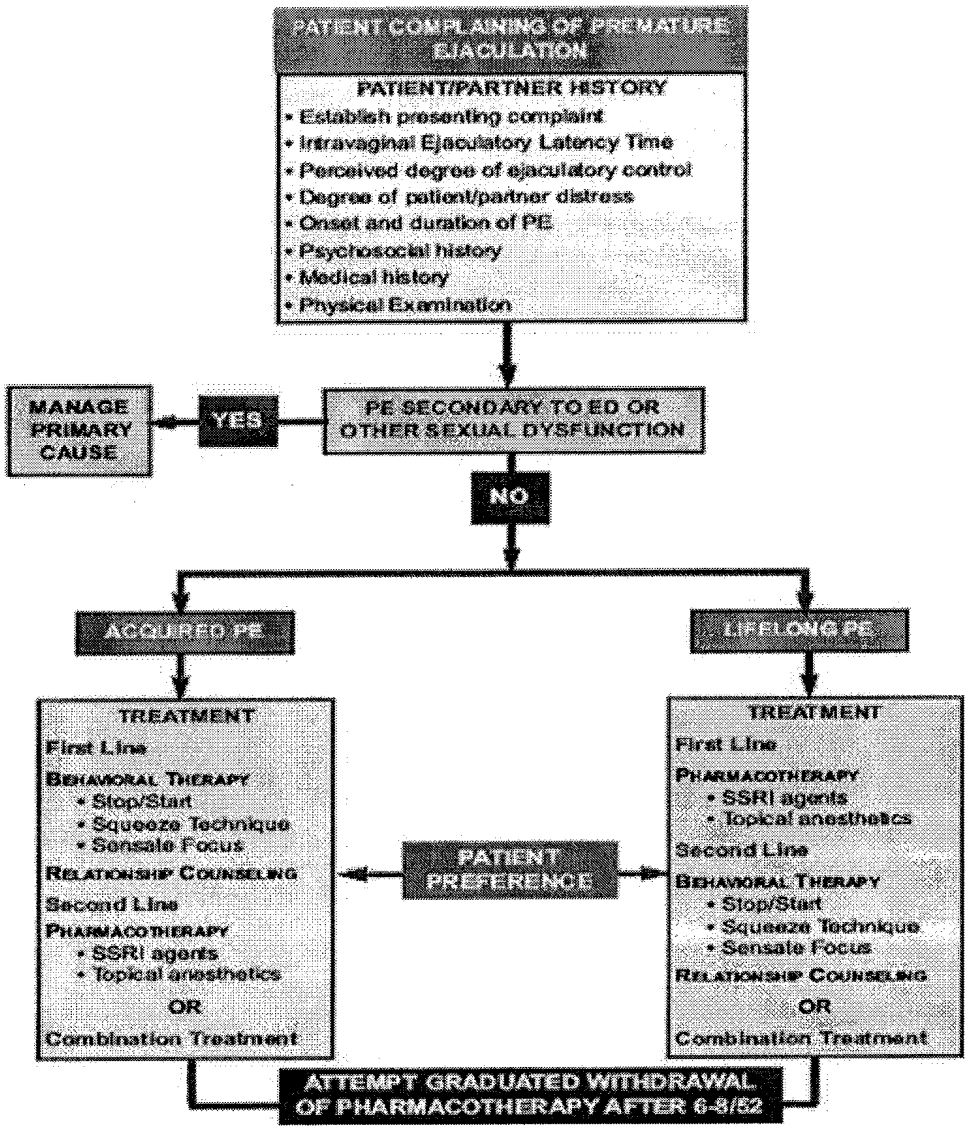

Figure 2, from McMahon et al., (2004), Figure 1

Evidence-based and expert-opinion consensus guidelines for the clinical management of men's sexual dysfunctions stress that erectile dysfunction must be distinguished from other sexual disorders, such as early or delayed ejaculation, anejaculation and lack of desire, although these disorders are frequently coexisting. *See* Lue, T.F., et al., Summary of the recommendations on sexual dysfunctions in men, *J Sexual Medicine*. 2004 Jul;1(1):6-23 at page 7, left column, which is a summary of the recommendations concerning men's sexual dysfunctions presented at the 2nd International Consultation on Sexual Medicine in Paris, France, June 28-July 1, 2003.

A companion consensus summary provides recommendations and guidelines concerning the state-of-the art knowledge for management of premature ejaculation, inhibited ejaculation, anejaculation, retrograde ejaculation and anorgasmia in men. *See* McMahon, C.G., et al., Disorders of Orgasm and

Ejaculation in Men, *J Sexual Medicine*, 2004 Jul;1(1):58-65, also a consensus summary from the 2nd International Consultation on Sexual Medicine in Paris, France, June 28-July 1, 2003. The algorithm for the diagnosis and treatment presented by McMahon et al. (2004) is provided in Figure 2, above.

The algorithm distinguishes primary PE from PE secondary to another sexual dysfunction. There are three drug treatment strategies to treat premature ejaculation described: 1) daily treatment with selective serotonin reuptake inhibitors ("SSRIs" such as citalopram, fluoxetine, fluvoxamine, paroxetine and sertraline); 2) as-needed treatment with SSRIs; and 3) topical local anesthetics (McMahon et al., page 60, right column). Although there have been several reports of experience with sildenafil citrate (Viagra®) as a treatment for PE, McMahon et al. deem it unlikely that such phosphodiesterase inhibitors have a significant role in the treatment of PE with the exception of men with acquired PE secondary to comorbid ED (McMahon et al., page 61, right column).

The Applicant respectfully submits that the combination of consensus summaries such as the Droller, Lue et al. and McMahon et al. references provides a more realistic measure of the prior art than the combination of the cited Yeager et al. and Kifor et al. references.

In a report of a study comparing SSRI (sertraline) treatment of patients with primary PE alone and patients with PE secondary to ED that was being successfully treated with sildenafil, sertraline effectively treated the patients with primary PE, but **PE that developed after sildenafil treatment for ED** did not respond as well to sertraline. *See* Chia, S.J., Management of premature ejaculation – a comparison of treatment outcome in patients with and without erectile dysfunction, Int. Journal of Andrology, 2002, 25:301-305, at page 304, right column. As noted above, the Office Action asserts that one of ordinary skill in the art would use a pharmaceutical composition for treating ED with the expectation of successful treatment of PE (Office Action, sentence spanning page 4, lines 8-12) However, one of ordinary skill who was aware of the Chia (2002) prior art would know that an effective treatment for ED, sildenafil (Viagra®), would not only be likely to produce secondary PE, but also would be likely to reduce the effectiveness of concomitant treatment of the secondary PE with an SSRI.

For the reasons discussed above, the teachings of Kifor et al., whether alone or in combination with Yeager et al., do not render the instant claims obvious. Reconsideration and withdrawal of the rejections under 35 USC § 103(a) is respectfully requested.

If at any time a telephone discussion would assist the Examiner and/or advance prosecution, please contact the undersigned.

This paper is being filed timely as it is being filed with a request for a three month extension of time and appropriate fees. In the event any additional extensions of time, fees and/or credits are necessary, please consider this a conditional petition therefor. The undersigned hereby authorizes the requisite fees to be charged and/or credited accordingly to Deposit Account No. 50-1582.

Respectfully submitted,

September 26, 2008

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